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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,742	01/28/2002	Henry Yue	PF-0728 USN	6026

22428 7590 07/15/2004

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EXAMINER	
KAM, CHIH MIN	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 07/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,742	YUE ET AL.Q	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-7,9-11,13,15-17,25,26 and 28-32* is/are pending in the application.

4a) Of the above claim(s) *10,25,26,28-30 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5-7, 9-11, 13, 15-17 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-3, 5-7, 9-11, 13, 15-17, 25, 26 and 28-32 are pending.

Applicants' amendment, Declarations of John C. Rockett, Tod Bedilion, and Vishwanath R. Iyer, and references filed April 26, 2004 are acknowledged. Applicant's response and the Declarations have been fully considered. Claims 1, 11 and 16 have been amended. Applicants request claims 25, 26, 28 and 32 be rejoined and examined upon allowance of the claims drawn to the polynucleotides and the polypeptides, since the claims of the polynucleotides and the polypeptides are not allowable in this Office Action, claims 25, 26, 28 and 32 along with non-elected claims 10 and 30 remain withdrawn from consideration. Therefore, claims 1-3, 5-7, 9-11, 13, 15-17 and 31 are examined.

Objection Withdrawn

2. The previous objection to the specification regarding the web address is withdrawn in view of applicant's amendment to the specification and applicant's response at page 12 in the amendment filed April 23, 2004.

Informalities

The disclosure is objected to because of the following informalities:

3. Applicants has amended Tables 1-4 to correct the "SEQ ID NO:" for the claimed polypeptide and polynucleotide in the tables, however, the amended Tables 1-4 do not include the whole content, thus they are entered. Applicant must submit Tables 1-4 with the whole content included. Appropriate correction is required.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

4. The previous rejection of claims 16 and 17 under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicant's amendment to the claim and applicant's response at pages 51-52 in the amendment filed April 26, 2004.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 1-3, 5-7, 9, 11, 13, 15-17 and 31 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

The claims are directed to a polypeptide of SEQ ID NO:11, or, a variant or fragment of SEQ ID NO:11 having activity of stimulating DnaK ATPase; a polynucleotide of SEQ ID NO:22 or a polynucleotide encoding the polypeptide; a cell comprising the polynucleotide; a method of producing the polypeptide; and a method of detecting a target polynucleotide containing the polynucleotide in a sample.

The specification discloses that the polynucleotide of SEQ ID NO:22 encodes the polypeptide of SEQ ID NO:11 (corresponding to SEQ ID NO:18 and SEQ ID NO:7 in Table 1), and SEQ ID NO:11 is a human chaperone protein (HCPN-11) which has sequence homology to the member of HSP40/DnaJ protein family (page 23). The specification also discloses the polypeptide of SEQ ID NO:11 (corresponding to SEQ ID NO:7 of Table 2) contains 269 amino acid residues, has DnaJ domains of E6-E71 and F12-S81, and exhibits DnaJ family signatures of A21-D40, E25-K41, F51-E71, R31-K90

and C104-F114; there is a DnaJ homolog, Hljip (S. cerevisiae) g972936 identified by BLAST search (see Table 2, SEQ ID NO:7); and the polypeptide variant has at least one functional or structural characteristic of HCPN (page 24). However, the specific function of the polypeptide of SEQ ID NO:11 is not identified. The specification asserts the claimed invention is useful in the diagnosis, treatment, and prevention of reproductive, eye, neuromuscular, metabolic, autoimmune/inflammatory disorders, infectious diseases, and cell proliferative disorders including cancers (page 1, lines 4-7 and page 23, lines 6-9; Table 3). The specification further asserts the claimed invention is useful for protein expression (page 54), as an antigen for producing antibodies (pages38-39), or for monitoring gene expression (pages 52-53). The claimed invention does not meet the utility requirement of 35 USC § 101 because the specification fails to assert a specific and substantial utility or to disclose a well-established utility for the claimed polynucleotide and polypeptide.

Regarding the asserted utilities of the diagnosis, treatment, and prevention of reproductive, eye, neuromuscular, metabolic, autoimmune/inflammatory disorders, infectious diseases, and cell proliferative disorders including cancers, it is noted that the specification fails to disclose a correlation between the claimed polynucleotide and/or polypeptide and a "specific" reproductive, eye, neuromuscular, metabolic, autoimmune/inflammatory disorders, infectious diseases, and cell proliferative disorder. Instead, the specification discloses the claimed compounds "may" be used in the diagnosis, treatment or prevention of a vast number of reproductive, eye, neuromuscular, metabolic, autoimmune/inflammatory disorders, infectious diseases, and cell proliferative disorders (see, e.g., pages 35-37 and 49-50) without providing any specific guidance as to

which of those disclosed diseases can be diagnosed, treated, and/or prevented using the claimed compounds. Even if the specification identified specific reproductive, eye, neuromuscular, metabolic, autoimmune/inflammatory disorders, infectious diseases, and cell proliferative disorders that can be diagnosed, treated, and/or prevented using the claimed compounds, the specification fails to provide the guidance necessary for diagnosing, treating, and/or preventing a particular reproductive, eye, neuromuscular, metabolic, autoimmune/inflammatory disorders, infectious diseases, and cell proliferative disorders. MPEP 2107.01 defines a "substantial utility" as a utility that "defines a 'real world' use" and that "utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities." In this case, further experimentation is required to use the claimed polynucleotide and polypeptide for diagnosing, treating, and/or preventing a reproductive, eye, neuromuscular, metabolic, autoimmune/inflammatory disorders, infectious diseases, and cell proliferative disorders. Therefore, this type of utility is not considered a "substantial utility". See Brenner v Manson, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966).

Regarding the asserted utilities of protein expression, for producing antibodies, and monitoring gene expression, it is noted that "any" polynucleotide can be used for protein expression, "any" polypeptide can be used as an antigen, and "any" polynucleotide can be used as a component of an array for expression analysis. MPEP 2107.01 defines a "specific utility" as a utility that "is specific to the subject matter claimed", which "contrasts with a general utility that would be applicable to the broad class of the invention." As the asserted utilities of protein expression, antigen for producing antibodies, and monitoring gene expression apply to the broad class of

polynucleotides and polypeptides, none of these utilities is specific to the claimed invention.

In response, Applicants traverse the instant rejection by arguing that the claimed polypeptide are identified as human cheperone proteins (HCPN), and the fact that the claimed polypeptide is a member of HSP40/DnaJ chaperone family alone demonstrates utility; and the claimed polynucleotide and polypeptide have use in toxicology testing, drug development, and the diagnosis of disease, without requiring knowledge of the function of the encoded polypeptide, as demonstrated in the Declarations of John C. Rockett, Tod Bedilion, and Vishwanath R. Iyer, and references submitted with the response (pages 12-15 of the response).

The response has been fully considered, however, the argument is not found persuasive because the specification fails to provide the guidance necessary for a skilled artisan to use the claimed invention for these asserted utilities, further research is required to identify or reasonably confirm a "real world" context of use for the claimed invention as explained in the section below. The examiner acknowledges that the utility requirement does not require knowledge of biological function of a claimed polypeptide and/or polynucleotide to satisfy the utility requirement of 35 USC § 101.

At pages 17-18 and 37-39, applicants argue that the claimed polypeptide is a member of the HSP40/DnaJ family of cheperones alone demonstrates utility because there is a substantial likelihood that the claimed HCPN is a member of HSP40/DnaJ family of chaperones as each member of this class is allegedly useful, the claimed polypeptide is similarly useful. Applicants argue that they have demonstrated by more than reasonable probability that HCPN is a member of the HSP40/DnaJ family of

chaperones which play roles in protein folding of newly synthesized proteins (page 2 of the specification; Table 2), and members of the HSP40/DnaJ family prevent the aggregation and misfolding of proteins, prevent non productive interactions with other cell components, direct assembly of multiprotein complexes and regulate HSP70 chaperones (see Fink, Physiol. Rev. 79, 425-449 (1999)). Applicants also argue that because there is no evidence that any member of this class of polypeptides would not be useful, it follows that the claimed polypeptide must by useful. Applicants' argument is not found persuasive.

There is no dispute that the sequence of SEQ ID NO:11 which contains DnaJ domains shares a high level of amino acid sequence identity with other members of HSP40/DnaJ family of chaperones in this region (Exhibit A, Blast search result). However, this relationship between the sequences does not confer patentable utility on the claimed invention. While the utility of the HSP40/DnaJ class of polypeptides is not at issue, it should be noted that there is no evidence of record to indicate that "all" members of this "class" of polypeptides have patentable utility; and even if SEQ ID NO:11 was classified as a HSP40/DnaJ, there is no indication that the claimed polypeptide has the same biological activity or the same use as other members of HSP40/DnaJ, e.g., DnaJ from E. coli (see Fink, page 429) considering the fact that the polypeptide of SEQ ID NO:11 (269 amino acids) is structurally distinct from other members of HSP40/DnaJ family (e.g., DnaJ from E. coli, 376 amino acids). Even assuming SEQ ID NO:11 were a member of HSP40/DnaJ family, the specification provides no guidance for using SEQ ID NO:11 in preventing the aggregation and misfolding of proteins, preventing non productive interactions with other cell components, directing assembly of multiprotein

complexes and regulating HSP70 chaperones. Thus, further experimentation would be required to determine the polypeptide of SEQ ID NO:11 is useful in the utilities applied to other members of HSP40/DnaJ family.

At pages 18-20 of the response, applicants argue evidence of "direct proof" of the utility of the claimed invention is provided by the Declarations of Dr. Rockett, Dr. Bedilion and Dr. Iyer, allegedly describing uses of the claimed invention in monitoring gene and protein expression, and assessing drug toxicity. Addressing the Rockett Declaration, applicants assert Rockett describes any expressed polypeptide or expressed polynucleotide is useful for a number of gene and protein expression monitoring applications, e.g., in 2-D PAGE technologies or cDNA microarrays, in connection with the development of drugs and the monitoring of the activity of such drug (Rockett Declaration, paragraphs 10-18). Addressing the Bedilion Declaration, applicants assert Bedilion describes any expressed polynucleotide is useful for gene expression monitoring applications, e.g., cDNA microarrays (Bedilion Declaration, paragraphs 4-7). Addressing the Iyer Declaration, applicants assert Iyer describes any expressed polynucleotide is useful for gene expression monitoring applications, e.g., cDNA microarrays (Iyer Declaration, paragraph 9).

It is noted that "any" polynucleotide can be used in a microarray. This asserted utility is not specific to the claimed invention. In this case, the specification fails to provide evidence that SEQ ID NO:22 or the polypeptide encoded thereby is a target for drug development, toxicology studies, or disease diagnosis. Furthermore, the specification fails to provide guidance for using the claimed compounds for drug development, toxicology studies, or disease diagnosis by expression analysis, e.g., how a

skilled artisan would use data relating to the claimed polynucleotide derived from the results of gene expression analysis and what the results would mean. As such, additional research is required to identify a "real-world" context of use for the claimed compounds. There is no dispute that the claimed polynucleotide can be used as a probe, however, this utility is not specific to the claimed polynucleotide. As one of ordinary skill in the art would recognize, any nucleic acid can be used as a probe – this utility is not specific to the claimed nucleic acid and instead applies to the broad class of nucleic acids. As stated in the section above, the examiner acknowledges and agrees that the utility requirement does not necessarily require knowledge of biological function as long as there is a specific, substantial, and credible asserted utility or a well-established utility for the claimed polynucleotide.

At pages 20-24 of the response, applicants argue that the claimed polypeptide can be used in protein and gene expression monitoring techniques such as 2-D PAGE and western blots, for assessing the potential toxic effect of a drug candidate, and Yue '742 application discloses the polynulceotide encoding the SEQ ID NO:11, are useful as probes in chips based technologies. At pages 24-34 of the response, applicants also argue that the use of polypeptides expressed by humans as tools for toxicology testing, drug discovery, and the diagnosis of disease is now well-established in view of the references cited at page 25 (U. S. Patent 5, 569,588; WO 95/21944; WO/95/20681; WO 97/13877; the Acacia Biosciences Press Release; the Glaser article), and the more genes and the polypeptides they encode, are available for use in toxicology testing, the more powerful the technique is. Applicants ' argument is not found persuasive.

The examiner agrees with applicants' arguments to the extent that, along with any other protein, SEQ ID NO:11 can be used in 2-D PAGE gels and western blots in drug toxicity monitoring – this non-specific use applies to the broad class of proteins. Although the use of the expressed polypeptides and polynucleotides in toxicology testing, drug development, and the diagnosis of disease is known in the art, the specification provides no guidance to allow a skilled artisan to use data relating to the claimed polypeptide derived from the results of toxicity testing and what the results would mean. For example, if the expression of the claimed polypeptide were monitored in a drug toxicity test, the specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. As such, further experimentation would be required to interpret the results of such expression analysis. A claimed polypeptide can meet the requirements of utility as long as the specification discloses a credible, specific and substantial asserted utility or a well-established utility for the claimed polypeptide, even though the function of the polypeptide is not disclosed in the specification.

At pages 35-36 of the response, applicants argue that a "real-world" utility exists if actual use or commercial success can be shown and that a showing of actual use or commercial success is conclusive proof of utility. Applicants argue that a vibrant market has developed for databases containing all expressed genes, including those of applicant's assignee, Incyte. Applicants state Incyte's customers and the scientific community have acknowledged that Incyte's databases have proven valuable, and that the databases including the claimed polynucleotide would be even more valuable. Applicants argue that customers can purchase the claimed polynucleotides from Incyte, saving the customer time and expense. Applicants' arguments are not found persuasive.

A rejection under 35 U.S.C. § 101 "for lack of operability" can be overcome by a showing of actual use or commercial success. The instant issue is whether or not the asserted utilities are substantial and specific. Such is not necessarily addressed by a showing of commercial success or actual use. Furthermore, there is no evidence to suggest that a database is any more or less valuable with the inclusion of the claimed compounds or that customers would desire to purchase the claimed compounds.

At pages 39-42 of the response, applicants argue the rejection is based on the grounds that the use of an invention as a tool for research is not a substantial use. Applicants state that only a limited subset of research uses are not substantial: those in which the only known use for the claimed invention is to be an object of further study, thus merely inviting further research. Applicants argue that nowhere in the cited case law is it stated or implied that a material cannot be patentable if it has some other, additional beneficial use in research. Applicants also argue the claimed invention has a beneficial use and that the claimed compounds are tools not an object of research. Applicants argue the data generated as a result of gene expression monitoring using the claimed invention is not merely to study the polynucleotide itself, but to study properties of tissues, cells, and potential drug candidates and toxin. Applicants also argue that without the claimed invention, information regarding properties of tissues, cells, and potential drug candidates and toxins is less complete. Applicants indicate the use of the claimed invention as a research tool in toxicology testing is specific and substantial since no two human expressed polypeptides or polynulceotides are interchangeable for toxicology testing. Applicants ' arguments are not found persuasive.

The claimed compounds do not provide specific benefit in currently available form, the claimed compounds have no well-established utility, and use of the claimed compounds would require further experimentation to identify a "real world" use. The claimed compounds are not disclosed as having a property that can be identifiably and specifically useful without further experimentation. The claimed invention is, in fact, the object of further study, merely inviting further research. None of the asserted utilities for the claimed compounds is specific and substantial and/or well-established. As previously stated, the specification fails to provide guidance regarding the interpretation of any results of expression monitoring using either the claimed polynucleotide or polypeptide and as such, further research is required to establish a "real-world" use for the claimed compounds. The specification provides no guidance to allow a skilled artisan to use data relating to the claimed polypeptide derived from the results of toxicity testing and what the results would mean. For example, if the expression of the claimed polypeptide were monitored in a drug toxicity test, the specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. As such, further experimentation would be required to interpret the results of such expression analysis. Regarding applicants' asserted use of the claimed polynucleotide for diagnostic assays, in order for a polynucleotide to be useful for diagnostic assay, there must be a well-established or disclosed correlation or relationship between the claimed polynucleotide and a disease or disorder. The presence of a polynucleotide in a diseased tissue is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed polynucleotide and the disease. If a molecule is to be used as a surrogate for a

disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polynucleotide to be used in a diagnostic manner. Many polynucleotides are expressed at equal levels and in identical forms in both normal *and* diseased tissues. In the absence of any disclosed relationship between the claimed polynucleotides or encoded proteins and any disease or disorder and the lack of any correlation between the claimed polynucleotides or the encoded proteins with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. Also, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form and would thus require further research for its implementation. Thus, the disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. § 101.

At pages 43-45 of the response, applicants challenge the legality of the Patent Examination Utility Guidelines. Applicants argue that "unique" or "particular" utilities have never been required by the law and applicants are unaware of any court that has rejected an assertion of utility on the grounds that it is not "particular" or "unique" to the specific invention. Applicants argue that to meet the utility requirement, the invention need only by "practically useful" and confer a "specific benefit" on the public. Applicants' arguments are not found persuasive.

Regarding the Training Materials, applicants are reminded that the examiner must examine a patent application according to the guidelines set forth by the USPTO as well as the MPEP, since the examiner has no authority to disregard such guidelines or to apply

his own interpretation of patent law in the examination of the application. Furthermore, as set forth in the guidelines and the MPEP, the guidelines were promulgated by the Patent Office in accordance with all applicable case law and thus are believed to be consistent therewith. Applicants are further reminded that the examiner has no authority to comment in regard to the legality of the new utility guidelines or the MPEP as set forth by the USPTO. Accordingly, it is the examiner's position that the instant claims, based on an analysis of the utility requirement of 35 USC § 101 and following the current Utility Guidelines, have no specific, substantial, or credible utility.

Regarding applicants' comments regarding a "unique" utility, it is noted that applicants' characterization of the examiner's position is misplaced. The examiner has not required applicants to identify a utility that is unique, i.e., not shared by any other compounds or compositions. Rather, applicants have been required to identify a utility that is "specific" to the invention claimed, as opposed to one that would apply regardless of the specific properties of the claimed invention. An invention certainly can have a utility that is shared by other compounds or compositions. While a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy 35 USC § 101.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 3, 6, 7, 9, 11, 13, 15, 16 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 3, 6, 7, 9, 11, 13, 15, 16 and 31 are directed to a polypeptide of SEQ ID NO:11, or, a variant or fragment of SEQ ID NO:11 having activity of stimulating DnaK ATP ase; a polynucleotide of SEQ ID NO:22 or a polynucleotide encoding the polypeptide; a cell comprising the polynucleotide; a method of producing the polypeptide; and a method of detecting a target polynucleotide containing the polynucleotide in a sample.

The specification indicates that the polynucleotide of SEQ ID NO:22 which encodes the polypeptide of SEQ ID NO:11 (Table 1); SEQ ID NO:11 which is a human chaperone protein (HCPN-11), contains 269 amino acid residues, has DnaJ domains of E6-E71 and F12-S81, and exhibits DnaJ family signatures of A21-D40, E25-K41, F51-E71, R31-K90 and C104-F114 (Table 2); and the polypeptide variant of SEQ ID NO:11 has at least one functional or structural characteristic of HCPN (page 24). However, the specification does not indicate which portion of the polypeptide is identical to SEQ ID NO:11, which fragment of SEQ ID NO:11 is biologically active, which portion of the polynucleotide is identical to SEQ ID NO:22, or which fragment of SEQ ID NO:22 encodes a biologically active fragment. There is no disclosure indicating all the sequences having at least 90% sequence identity to SEQ ID NO:11 are functional, and

the specification has not identified any biologically active fragment or variant of SEQ ID NO:11. Without guidance for structure to function/activity, one skilled in the art would not know which region or residue(s) of SEQ ID NO:11 is essential for function/activity and how to identify a functional polypeptide. The lack of a structure to function/activity relationship and the lack of representative species for the variant or fragment of SEQ ID NO:11, or the polynucleotide related to SEQ ID NO:22 which encodes the functional polypeptide as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

In response, applicants indicate that the present claims specifically define the polynucleotides and polypeptides through the recitation of chemical structure rather than functional characteristics, e.g., a polypeptide comprising a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence of SEQ ID NO:11 (claim 1), and cases such as *Lilly* and *Fiers* stress that the recitation of structure is an important factor to consider in a written description analysis of the claims; the present claims do not define a genus which is highly variant, in support of this assertion, applicants cite Brenner et al. (PNAS USA 95, 6073-6078 (1998)) which have determined that 30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues, and the variation in the claimed polypeptides is far less than the reliable threshold for establishing evolutionary homology between proteins; and the state of the art at the time of the present invention (priority date 10/22/99) is further advanced than that at the time of the *Lilly* and *Fiers* applications (1977), e.g., PCR, highly efficient cloning and DNA sequence technology are developed,

with these remarkable advances, one of skill in the art would recognize that given the sequence information of SEQ ID NO11 and SEQ ID NO:22 and additional detail provided by the instant application, the present inventor were in possession of the claimed polynucleotide and polypeptide variants (pages 46-51 of the response).

The response has been fully considered, however, the argument is not found persuasive for the reasons stated in the following: The specification has defined the polypeptide sequence of SEQ ID NO:11 and the polynucleotide of SEQ ID NO:22, however, it does not provide sufficient teachings on the variant, e.g., it has not specified which portion of the polypeptide is identical to SEQ ID NO:11 as to 90% sequence identity, and which portion of the polynucleotide is identical to SEQ ID NO:22 as to 70% sequence identity which encodes a polypeptide that stimulates DnaK ATPase activity, nor has identified any biologically active fragment or variant of SEQ ID NO:11. Even with the advanced technology in the recombinant DNA at the time of present application, the lack of guidance and teaching on the structure to function/activity relationship, one of skilled artisan would not know how to identify a functional polypeptide. Regarding the reference by Brenner et al., it appears applicants attempt to use teachings that clearly are not relevant to SEQ ID NO:11 to support their argument. Nowhere does the reference of Brenner et al. suggest that the disclosed results can be extrapolated for use in predicting functional homology of any protein. Moreover, one of skill in the art would recognize that such teachings do not apply to other proteins as Brenner et al. teach their comparisons "have been assessed using proteins whose relationships are known reliably from their structures and functions, as described in the SCOP database" (page 6073, abstract). Brenner et al. are silent as to the use of their results to the functional

assignment of an uncharacterized protein. Therefore, a skilled artisan would not recognize applicants were in possession of the claimed invention.

Conclusion

7. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

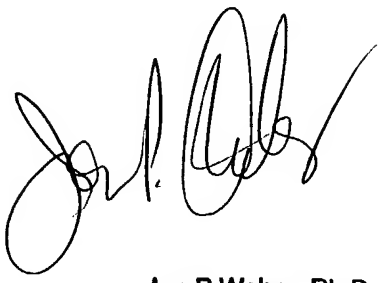
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner

CMK
July 6, 2004



Jon P. Weber, Ph.D.
Primary Examiner